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10/582,702	04/23/2007	Jeffrey Schlom	59849(47992)	4962

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EXAMINER	
GUSSOW, ANNE	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,702	SCHLOM ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-78* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 31-78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/12/06, 6/19/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence alignment*.

DETAILED ACTION

1. Applicant's election of Group 57, claims 14-30, drawn to a polypeptide comprising SEQ ID No. 19, in the reply filed on February 3, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-13 and 31-78 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on February 3, 2009.

3. The restriction requirement between Groups 38, 39, and 51-57, drawn to the polypeptides comprising SEQ ID Nos. 1, 2, and 14-19, is withdrawn because the peptide of SEQ ID No. 19 is identical to SEQ ID No. 2 and also reads on the additional sequences of SEQ ID Nos. 1 and 14-18. The restriction requirement between Groups 1-37, 40-50, and 58-158 is maintained.

4. Claims 14-30 are under examination.

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on June 12, 2006 and June 19, 2007 have been considered by the examiner and an initialed copy of the IDS is included with the mailing of this office action.

Specification

6. The disclosure is objected to because of the following informalities: the specification contains sequences in table 1 page 74, page 84, and figures 9 and 10 which are not identified by a SEQ ID No. and do not appear to have a SEQ ID No. in the sequence listing as filed. See 37 CFR §1.821-1.825

Appropriate correction is required.

7. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The browser executable code is on page 24 of the specification.

8. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

9. The use of the trademark Xeloda™ has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

10. Claim 15 is objected to because of the following informalities: The claim contains a typographical error. Appropriate correction is required.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 14-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to isolated polypeptides comprising an amino acid sequence of SEQ ID Nos. 1, 2, or 14-19 or fragments or variants thereof. The claims are also drawn to agonist polypeptides which are at least about 60%, at least about

80%, at least about 90% or up to about 99.9% identical to the amino acid sequence of SEQ ID Nos. 1, 2, or 14-19 (emphasis added). Claims 17-26 are included in this rejection because they depend from claim 14.

The specification discloses peptides of SEQ ID Nos. 1, 2, and 14-19 which are epitopes of MUC1. The specification discloses mutations at specific positions in the sequences to maintain the function of the polypeptide (see table IV, page 77 of the specification).

The specification does not provide sufficient written description as to the structural features of the claimed genus of polypeptides and the correlation between the chemical structure and function of the genus of polypeptides, such as structural domains or motifs that are essential and distinguish members of the genus from those excluded. The specification does not disclose a complete deletion mutation analysis to describe the broadly claimed genus of polypeptides which have up to 99.9% identity, thus having only a single amino acid residue in common with SEQ ID No. 1, 2, or 14-19.

A "representative number of species" means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir.

2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004)(Claims directed to PTFE dental floss with a friction-enhancing coating were not supported by a disclosure of a microcrystalline wax coating where there was no evidence in the disclosure or anywhere else in the record showing applicant conveyed that any other coating was suitable for a PTFE dental floss.).

It has been well known that minor structural differences even among structurally related compounds can result in substantially different biology, expression and activities. Based on the instant disclosure one of skill in the art would not know which residues are essential, which residues are non-essential and what particular sequence lengths identify essential sequences for identifying an agonist polypeptide encompassed by the claimed specificity. For example, there is insufficient guidance based on the reliance of disclosure of SEQ ID Nos. 1, 2, and 14-19 to direct a person of skill in the art to select or to predict particular sequences as essential for identifying agonist polypeptides encompassed by the claimed specificities. Additionally, there is no art recognized correlation of the instantly claimed polypeptides and their function. Mere

idea of function is insufficient for written description; isolation and characterization at a minimum are required.

Skolnick et al (Trends in Biotechnology, 2000. Vol. 18, pages 34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based on sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to function of the structurally related protein (see in particular "Abstract" and Box 2).

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology, 1990. Vol 111, pages 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology, 1988. Vol 8, pages 1247-1252).

In the absence of sufficient guidance and direction to the structural and functional analysis, applicant's reliance on the activity of the agonist polypeptides of SEQ ID Nos. 1, 2, and 14-19 disclosed in the specification as-filed does not appear to provide

sufficient written description for the genus of polypeptides encompassed by the claimed specificities in view of the above evidence, which indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed.

For inventions in an unpredictable art, adequate written description of a genus, which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case, applicant has not disclosed the common attributes or features (i.e., structural domains) that are essential for activity or those which are non-essential. See, e.g., Eli Lilly. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. If a representative number of adequately described species are not disclosed for a genus, the claim to that genus must be rejected as lacking adequate written description under 35 U.S.C. 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the

method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddles v.Baird*, 30 USPQ2d 1481, 1483. In *Fiddles v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides of SEQ ID Nos. 1, 2, and 14-19, but not the full breadth of the claim meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 101

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claims 27-30 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 27-30, as written, do not sufficiently distinguish over polypeptides as they exist naturally because claims 27-30 do not particularly point out any non-naturally

occurring differences between the claimed polypeptides and the structure of naturally occurring polypeptides.

In the absence of the hand of man, the naturally occurring polypeptides are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" polypeptide or similar language would obviate this rejection.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Gendler, et al. (Journal of Biological Chemistry, 1990. Vol. 265, pages 15286-15293, as cited on the IDS filed June 12, 2006).

The claims recite an isolated polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 1, 2, or 14-19, fragments or variants thereof. Gendler, et al. teach an amino acid (polypeptide) sequence of mucin 1 which comprises the sequences of

SEQ ID Nos. 1, 2, and 14-19. The sequence of Gendler, et al. reads on the instant sequences because the claims are drawn to polypeptides which comprise the sequences of SEQ ID Nos. 1, 2, and 14-19, thus, the claims read on the full length mucin 1 amino acid sequence. Since the claims are not limited to the sequence of SEQ ID Nos. 1, 2, or 14-19 and Gendler, et al. teach a polypeptide which comprises SEQ ID Nos. 1, 2, and 14-19, all the limitations of the claims have been met.

17. Claims 14-17 and 20-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson and Ramshaw (WO 01/90197, published November 29, 2001).

Claims 14-16 have been described supra. Claims 17 and 20-30 recite the isolated polypeptide of claim 14, wherein the polypeptide binds to HLA molecules with a high avidity, wherein the polypeptide is derived from a mucin tumor antigen, wherein the polypeptide is derived from a non-variable number of tandem repeats region of MUC-1, wherein the polypeptide induces an immune response, wherein the immune response is a cellular immune response, wherein the cellular immune response is a cytotoxic T cell response, wherein the cellular immune response is a T helper cell response, wherein the cellular immune response is a B cell immune response. An agonist polypeptide comprising an amino acid sequence which is at least about 60% identical to the amino acid sequence of SEQ ID NO: 1, 2, or 14-19. An agonist polypeptide comprising an amino acid sequence which is at least about 80% identical to the amino acid sequence of SEQ ID NO: 1, 2, or 14-19. An agonist polypeptide comprising an amino acid sequence which is at least about 90% identical to the amino acid sequence of SEQ ID

NO: 1, 2, or 14-19. An agonist polypeptide comprising an amino acid sequence which is up to about 99.9% identical to the amino acid sequence of SEQ ID NO: 1, 2, or 14-19.

Thomson and Ramshaw teach a polypeptide derived from MUC1 that comprises the sequence of SEQ ID No. 1, comprises a sequence that is 90% identical to SEQ ID Nos. 2, 14, 16, and 19 (one amino acid substitution) and comprises a sequence that is 80% identical to SEQ ID Nos. 15, 17, and 19 (two amino acid substitutions) (see sequence alignment). Thomson and Ramshaw teach peptides are recognized by HLA (page 3) for induction of an immune response to activate both T cells and B cells (pages 89-90). Regarding the agonist polypeptide, the specification defines an agonist polypeptide as epitopes in the polypeptide which activate a stronger immune response than a native polypeptide (page 33). The sequence of Thomson and Ramshaw is not the entire native polypeptide and since Thomson and Ramshaw were isolating polypeptides for the express purpose of generating an immune response one of ordinary skill in the art would expect the polypeptides of Thomson and Ramshaw to be an agonist polypeptide as defined by the instant specification. Since the claims are not limited to the sequence of SEQ ID Nos. 1, 2, or 14-19 (polypeptide comprising SEQ ID No.) and Thomson and Ramshaw teach polypeptides which comprises SEQ ID Nos. 1, 2, and 14-19 for induction of a T cell or B cell immune response, all the limitations of the claims have been met.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
March 26, 2009

/Anne M Gussow/
Examiner, Art Unit 1643